CENTER FOR GLOBAL DEVELOPMENT

MAKING MARKETS FOR VACCINES: FROM IDEAS TO ACTION

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P R O C E E D I N G S

MS. BIRDSALL: Good morning, ladies and gentlemen. Thank you very much to all of you for being here for what I know is going to be a very exciting morning.

I'm Nancy Birdsall. I'm the President of the Center for Global Development, and I'm very proud and pleased today to see you and to have this opportunity to talk about something that is so important to so many people in the world.

Many of you know that the Center for Global Development has a mission. It's a grand one. It's to reduce poverty and inequality around the world with a focus on developing countries. We do that largely by worrying about, agitating about and engaging in how to improve the policies and practices of the rich world, the rich countries and the global institutions that deal with problems of the global system.

I want to start by giving a very warm thanks to Covington & Burling, you'll be hearing in a few minutes from some of the distinguished folks at Covington & Burling, not only for providing this lovely space for us this morning, but for participating with three expert members in the working group whose work we're talking about today. Those three lawyers who participated along with many others who engaged with the working group deserve our warm thanks.

Today we're going to be hearing about a proposal to deal with what is a really vexing problem. If you're here, you're probably already familiar with it. It's the problem and the challenge of how to realize the tremendous scientific potential that exists and that can be provoked for improving the lives of people in the developing world. That's the connection, of course, to the mission of the center.

We're particularly concerned at the center with the problem of providing, financing, managing global public goods, and managing global bads, of course. Everyone knows about the global public bad of greenhouse gas emissions. I don't think enough Americans and Europeans and Japanese know enough about the potential global public good of developing medicines, vaccines, that would save millions of lives in the developing world.

This kind of problem of generating public goods we manage in our countries reasonably well. We don't really have the institutions and infrastructure at the global level to manage those problems sufficiently, and that's what we're talking about today, is finding a way to create an infrastructure and/or an institution in the broadest sense that would address this vexing problem.

You all probably know that this working group took an idea, instituted, initiated, by Michael Kremer of Harvard whom you'll be hearing from in a few minutes. The group was led by my distinguished colleague Ruth

Levine, and by Alice Albright. All of them you'll hear about in the next few minutes.

What they did in the working group is they took an idea that had been developed by Michael, fleshed it out even more, and have put it on the table. It's a table that's been set. I think the challenge for us in the next months and years is to ensure that some people and some institutions get to the table and think about and can soon internalize this idea.

We're very pleased that even in the short space between the completion and finalization of the working group report and today there has already been in the air and from policy makers a lot of interest. Gordon Brown, as many of you know, from the U.K. picked up the idea, and the United States Council of Economic Advisers has highlighted in a report the need to deal with the problem of low, insufficient research and development for certain medicines.

Let me say one more thing which is the morning will have three parts. We are going to hear some keynote addresses. Then we will have a presentation of the content of the working group report. Then we will have a very distinguished panel.

I'm reminded to say that we have really a lot of stories today that you'll be hearing, but what's interesting to me is we have a lot of stories in the audience, too. This is not only a high-powered group of speakers and panelists, but it's a high-powered audience. So we look forward, I certainly do, to hearing your comments and questions when we come to that part after the panelists have spoken.

I now have the pleasure of introducing to you Peter Hutt. Peter Hutt is here at Covington & Burling, and it is to him that we owe the privilege of being here today.

MR. HUTT: On behalf of our law firm I'd like to welcome all of you today.

I've been privileged to serve as a member of the working group and my partner John Hurvitz who you'll hear from has been working very hard on the issues of how one implements this report.

All of us believe very strongly in this. We have provided our services on a pro bono basis for this entire effort because we can think of nothing more important than providing safe and effective new vaccines for the diseases that ravage the developing world.

I will keep my remarks very brief this morning. I welcome you again, and I am privileged to have participated in this. Nancy, I'll turn it back over to you.

MS. BIRDSALL: We can see how valuable the time is of Covington & Burling lawyers. Thank you very much, Peter.

Now I introduce to you for any of you who don't already know him or know of him, Rick Klausner who directs the Gates Foundation's Global

Health Program which has a mission not unlike that of CGD which is to improve global equity.

Rich was the Director of the National Cancer Institute. He oversaw the creation and development of the Vaccine Research Center. He is from a part of the world that I come from, metropolitan New York City. We have some mutual friends, so I asked him, where are you from, Rick, exactly? All I can remember him saying is, it's something about Woody Allen.

So Rick is not a Woody Allen type. He is more of a serious guru, but he does have a good sense of humor. So it's really been a pleasure to work with him and to work under his sponsorship at Gates.

MR. KLAUSNER: Nancy, thank you very much, and it is really a pleasure to be here. This is an important and in many ways historic discussion that we're having.

The fact that so many people are in this room from industry, from the private sector, government, academia, represents a real triumph in a maturation of our approach to global health and global equity.

First of all, I want to congratulate the Center for Global Development. I particularly want to congratulate all who worked on this working group. This working group is part of an initiative that the Gates Foundation has the privilege of funding called the Global Health Policy Research Network which has its home at the Center for Global Development, and it's led by Ruth Levine. It works through a whole variety of mechanisms including a series of policy-specific working groups such as the one today.

We at the Gates Foundation have turned to the Center for Global Development as a really great partner. We see them both as an incredible source for innovation, innovation in ideas and policy, and most importantly, in actionable evidence-based approaches particularly aimed at moving donors beyond empty rhetoric to real action. That's very much what we're here about today, something based upon careful thought and action, motivated by moral imperative which is easy to talk about, but translatable into real change. I particularly want to recognize Michael Kremer, Alice Albright and Ruth Levine who led this particular working group.

So what are we here to talk about? For the developing world, the market forces that--the production of critical health technologies have failed. They fail financially in that there is inadequate purchase power. They fail in terms of markets functioning with predictability, particularly predictability of demand and, therefore, of supply, and who intermediates and demand, purchasers.

Finally, and this is critical as pointed out in the report you'll hear about, they fail at the level of delivery. There are few guides throughout the complexity of what we call the developing world to ensure that critical connectivity that must link supplier, purchaser and ultimately the consumer.

These three barriers of market failure have to be addressed. What we're talking about today is one aspect of addressing, dealing with resource, dealing with predictability, and that must take place in the context of a new connectivity that links the creators of critical health interventions with the ultimate consumers.

The new ethos of global health is one that sees market or market-like mechanisms and industry involvement as essential parts of solutions to global health and equity. Certainly at the Gates Foundation, we have this very strong belief that these issues are solvable, that the fact that they relate to poverty is no excuse to preventing us from solving health and equity problems, and there is fundamentally a critical role of both the public sector and the private sector.

The question is how do we as the global health community bridge the needs for sustainable solutions with the fact of market failures. This is where creative approaches to market enhancement or partial market replacement be it public or nonmarket interventions come in, and, again this is why we are here today.

The report that you'll be hearing out produced by the working group provides us with a new and incredibly valuable tool for helping donors think about how to build market-like incentives or market incentives to encourage industry to invest in the development of products for the world's neglected diseases.

I don't need to go through the statistics of the level of need and the level of neglect. We need that sustainable solutions require both new technologies, technologies that address ignored problems, and technologies that have the characteristics of being deliverable which is not the same. There are two aspects of technologic development. But also that we need to bring market forces to bear, market forces that have in this space the intervention of governments and other nonmarket sources.

These two, the development of technologies and the role of market forces to help in the delivery of those technologies and their development are fundamentally interrelated. As many of you know, we talk about push mechanisms to help stimulate the creation of technologies and pull mechanisms to assure that market-like mechanisms assure that they are both created and can be delivered, and these two must work together.

This report, and as Nancy said, the follow-on work that must be done, will help initiate an exploration of shaping the market today can help us speed and shape investment into innovation in new technologies of the future.

At the Gates Foundation we see our own role as catalyzing and helping to fund the development of both. It is true that much of our investment in the foundation helps fund the development of deliverable technology through push mechanisms. But also, a significant amount of our attention is aimed at policy, financing mechanisms, that are so perfectly

captured by the work of this working group, to look at the range of pull mechanisms market-like incentives that will pay dividends today and in the future.

We already see in global health that pull mechanisms work. Many of you are familiar with something called the Global Alliance for Vaccines and Immunization, GAVI, and its associated fund called the Vaccine Fund. This is a mechanism that is working. It is push-pulling the creation of new products such as hepatitis B vaccine, one of the typical disasters of the gap between the introduction of technologies in the rich world and 20 or more years of delay before an affordable, essential vaccine is delivered to the developing world.

With this purchase fund we have seen in just 3 years the movement from an inadequate supply by only a single global manufacturer in terms of the combination vaccine, to now something like eight to 12 suppliers. Demand has gone up. Supply is about to catch up to the greatly increased demand. In that process through this pull mechanism, prices dropped by about 20 percent. Pull mechanisms can work.

If donor countries led by the United Kingdom and France and others are successful in launching the much recently talked about International Financing Facility for Immunization to use securitized bond financing to raise over $4 billion over 10 years, this may also change the scale and scope of today's opportunities to create pull incentives for today's and tomorrow's products.

This specific report prevents a convincing argument that we may now have one more specific tactic, a new tool, for pulling in this case vaccine development, signaling purchase in advance through bilateral contract mechanisms in order to stimulate competition and to produce the desired product. There are many critical questions about this that this report does a fantastic job of answering.

Is an advanced purchase contract legally possible? Yes, and you'll hear about that. Can they be structured in a way that continues to encourage innovation? Would we be able to implementing in the existing global health landscape the important analytic work that this group has given us very important insight and answers to these critical questions, is this doable?

There are of course questions that remain unanswered. Now will we measure the impact of these incentives? Will they have equal impact for both late and early stage products? How would you price these contracts given other incentives of funding in the market? These are details that within this critical framework I am convinced can be worked out.

We hope that this leads to a field of study and action and work that explores the range of tools that we should be using required to change the landscape of market incentives for the introduction and production of new drugs, new vaccines, diagnostics and other critical health interventions that

characterize and underlie the incredible health that we all take for granted that is simply not shared by at least half the people with whom we share this planet. So as we move forward from today, we have a lot of both questions to answer and work to do.

As with any new mechanism, we need to explore the details. We need to recognize that health technologies are complex. There is no one-size-fits-all, and the work today provides in fact a flexibility of approaches that will need to be applied as a function of the particular product, where it is, are there tiered markets, in other words, dual markets, both rich world markets and poor world markets? As I said, what stage of development? What do we know about the R&D bottlenecks to create deliverable health technologies?

We need to deal with the political realities of donor governments making long-term commitments or promises, but we see as Nancy said great encouraging motion in this area led recently by Gordon Brown of the U.K., but there are lots of other things going on. Chuck Ludlum (ph) is here. He and Senator Lieberman in discussing Bioshield provides a whole, it's not exactly the same with this, but another set of really important activities and thoughts about pull mechanisms and policy tools for changing the landscape where markets have failed for critical health interventions.

We need to look at the range of pull mechanisms and realize that we need a range of tactical approaches to pull, and we need to continue to understand the intersection between pull and what we call push. This is an outstanding piece of work and we are very proud to have been able to be both involved intellectually and to have been able to support this.

With it, the conversation about global health has moved forward in both creativity and sophistication. No longer in global health can there be or is there the old divisions between the private sector and public goods. There is a recognition of the need to link those to everyone's benefit.

It is now incumbent upon all of us engaged in this to not let this conversation lapse, and to build upon this rapidly at the level of making policy, making decisions, because there are products available that are simply not savings the lives that could be saved now and must be saved in the future. Thank you.

MS. BIRDSALL: Thank you very much, Rick. We all know the Gates Foundation is very rich, but the key to the Gates Foundation, and I like to think it's the same for our small Center for Global Development, is not the wealth in dollars, but the wealth in ideas and a tremendous ability to leverage those ideas and dollars as you heard from Rick. He said this is an actionable idea. It calls to mind the subtitle of the working group report, "Ideas to Action."

I am happy to introduce to you Scott Whitaker. He is the Executive Vice President and the Chief Operating Officer of the biotechnology

organization BIO. He had the difficult job I can imagine of being the chief of staff to Secretary Thompson at HHS which he left I guess just very recently.

He there managed not only all the operations of the department day to day, but all the major policy and management issues. You can imagine it was an exciting job.

Before that he served on the staff of Senator Don Nickles, Senate Assistant Majority Leader, in various capacities, including eventually as policy adviser for the Office of the Assistant Majority Leader.

MR. WHITAKER: Thank you very much. I apologize. I've got a little bit of a cold this morning, so if I cough a little bit, I'll try not to turn to my left to Rick doesn't catch it.

Jim Greenwood was supposed to be here today, and I am here to deliver his remarks for him. He regrets not being here for a couple of reasons. One, this is an issue he cares about deeply and the industry that we represent cares about a great deal as well. But secondly, his home has been flooded, and the weather over the past weekend flooded out his home in Bucks County, Pennsylvania. He's at home digging out from the flood as the family has been relocated. So it's a difficult situation for Jim. But he was insistent that I come today and share his remarks because of how important this issue is to him.

I'm sure he doesn't feel fortunate today as the flood has spread through his area of Pennsylvania, but it is a reminder of how fortunate we are in this country isn't it? When a flood simply means relocation of our house and insurance claims and things like that and we don't have to worry about things like dirty drinking water and possible epidemics that break out as a result of those disaster, where we live makes all the difference. It makes a great difference in every day health care, and especially with the subject we're discussing today.

For our country's deadliest and most disabling diseases such as cancer and heart disease and diabetes, we have an array of technologies, a health care infrastructure that gets those technologies to us when we need them, and an R&D system, frankly, that's well funded and racing to create the next generation of new drugs and devices and diagnostics and vaccines.

But what we're here to talk about today are potential solutions to global health crises that, frankly, are in many ways are bigger than cancer, bigger than heart disease, and bigger than diabetes.

Many of you are familiar with our 90/10 problem that we often talk about at BIO. It's frequently invoked that 10 percent of biomedical research and development dollars are directed toward infectious diseases that constitute 90 percent of the global burden, and much of what is being discussed here today addresses that issue.

Rick didn't talk about the statistics, but I want to mention just a couple of them. For the world's poorest, infectious disease has a devastating

toll. Malaria kills a child every 20 to 30 seconds. HIV and AIDS afflicts 25 million people in sub-Saharan Africa. Tuberculosis infections, many of them are becoming more drug resistant and are soaring after decades of decline. Impoverished nations continue to be racked by diarrheal disease, pneumonia, tropical aliments and many, many other things.

The top five diseases along cost more than 10 million lives each year and disable tens of millions more, so it's a serious problem.

My former boss, Secretary Thompson, used to say this, "As overwhelming as the statistics are, the tragedy is brought into terrible focus when you sit down face to face with individuals who are suffering in Third World or developing countries." You see a woman suffering with AIDS. You see kids who have lost both parents to diseases that have wrecked their lives. And you meet with the health care workers over there that have struggled to find the tools necessary to combat the spread of disease. In some of these societies children are losing their parents, businesses are losing their workers, individuals are losing their teachers, doctors and farmers. Entire countries are losing their next generations of leaders. It's a critical problem for a variety of reasons that need to be addressed.

What does that mean to us here today? What does it mean to the biotech community? It highlights the importance of this report, frankly. It tells us why this event is so important to us today. Let me talk to you a little bit about BIO.

The biotechnology industry which BIO represents here in Washington has done a lot to be helpful. We can't solve the Third World health care problem alone, but we are trying to do our part to address the health care problems and the crisis.

Disease is a biological problem. Biotechnology offers biological solutions. Gnenomics proteomics allow us to understand bacteria, viruses and parasites as well as other human responses to these invaders. Biotechnology can create highly targeted approaches preventing and treating infections such as recombinant vaccines and antibodies. Many biotech companies are developing drug delivery devices and technologies today that can eliminate the need for cold storage, needles and other infrastructure requirements that make it very difficult to bring vaccines and medicines to market.

In 2002, BIO brought together companies developing these technologies with nonprofits in the U.S. and international health agencies to discuss the global health crisis and collaborate together on what biotechnology could do to help. Out of those discussions emerged Bio Ventures for Global Health.

On behalf of Mr. Viva (ph), let me just thank you, Rick, and the Gates Foundation for what they've done to help us with that in funding some of our work. And Wendy Taylor is here as well. Wendy is the Executive Director of our Bio Ventures Initiative at Global Health. She was a former

BIO employee. We'd like to still think of her as a BIO employee, but she's done a great job addressing this problem.

Bio Ventures has treated global health as a business from the outset and sought ways to create market-based business models that would foster global health research and development. Because Bio Ventures grew out of BIO, they knew the business of biotechnology very well.

Let me tell you just a little bit about that business. The biotechnology industry consists of more than 4,000 companies worldwide all of which are chasing a limited pool of investment capital. More than half of these companies employ 50 or fewer people and more than 90 percent have yet to bring a biomedical product to market. These are small businesses, but they're doing big science.

They're developing therapies and vaccines at a cost of hundreds of millions of dollars per product, and along the way they and their investors are taking huge, huge risks. Only 8 percent of drugs in interclinical testing are ultimately approved.

To attract capital which Rick talked a little bit earlier, biotech companies have to show their investors that the financial risk is going to be rewarded with high returns if a product does in fact succeed. As in the movie business, only a handful of funded projects ever really turn in a profit, and even fewer will become the blockbuster drugs and treatments that investors keep coming back for.

The challenge for biotechs interested in the developing world is that the market for successful products is too small even for diseases that afflict millions. According to a former head of a vaccine company and now a venture capitalist, he said companies only kick into gear when there's a market pull, and Rick talked about this in a great amount of detail.

In the developing world there is simply no market pull for many of the drugs and therapies that are needed, and vaccines that are needed. The world's least-developed nations spent $17 per capita per year on health. Other low-income countries spend an average of $36. High-income regions, Europe, Japan and some of the other areas, spend more than 60 times that much per capita.

Fortunately, vaccines are relatively cheap given the benefit they provide. The United States contributed, for example, $32 million in the 1970s effort to erase the scourge of small pox from the earth, and it was effective. According to the Institute of Medicine in the late 1990s, that investment has yielded a return of $32 million every 26 days. Every dollar spent on measles, mumps and rubella vaccines is found to save $21. So it's an example of how effective vaccines and research can be.

Yet vaccine research in many ways has decreased in the United States in the '80s and the '90s. Production of existing vaccines in many cases fell sharply. Pharmaceutical companies in many cases flood the business in

part because government and international agencies have set prices for existing products too low and there simply wasn't a market demand.

Today the entire global market for vaccines, the products with the most potential impact on poor countries, is about $6 billion, about 1.5 percent of the amount that's spent on pharmaceuticals. And the total developing world market for vaccines is only about $500 million a year.

Given the limited pool of talent and investor capital, biotech companies cannot devote their resources to disease for which there is very little or no market, and that's what causes such a challenge for our companies.

For biotech CEOs like Russell Howard at Maxigen (ph) who worked on diseases of this nature, he said research of this nature is always set off to the side. His company worked on vaccines for dengue and malaria and HIV, but progress was very slow, funded with a patchwork of grants and nonprofit partnerships and a little bit of investor money which were directed, but at the same time had great risk.

So that's what's so exciting about what we're talking about here today. Today we're excited about the work that's been done. The report that's being unveiled today is a new model for breaking the impasse at companies like Maxigen and dozens of others of our companies who need help and need investment.

The report released today offers a template for industrialized countries to create markets for global health products through air-tight advanced purchase commitments that restarts a much needed debate on the critical issues, and it's very, very important.

The commitments must be air tight because it takes 10 to 15 years for a vaccine or drug to be developed. Biotech companies must be certain that if a product succeeds, there is going to be money at the end of the day for them. The commitment outlined today is a realistic commitment, something that should be discussed and deserves a great amount of attention not only in this town but throughout the world.

Of course, an idea is only the beginning isn't it? The next step will really be making the case for participation in industrialized countries. In an era of tight budgets and aging populations with growing health care demands, law makers may ask why should they spend such precious research dollars on diseases that don't necessarily affect their constituents.

First and foremost, there's a humanitarian reason for doing this isn't there? Americans, Europeans and other nations have a history of rising to the occasion where there are emergencies, when there are health crises, when there are major problems. Just think, the top five diseases alone take a toll equivalent to 50 tsunamis every year.

Secondly, there is self-interest at play. With 2 million crossing international borders every day and more than a million each week traveling

from developing to developed nations, it is in our interest to do this research and do this investment to protect our citizens as well.

In fact, since 1973, at least 30 infectious disease agents have surfaced, while more than 20 have expanded to other geographic regions. But none of these most deadly diseases have become a pandemic as a result of a combination of good luck and an aggressive public health response to the emerging diseases. Industrialized nations, especially the U.S., also care deeply about stability and security. Countries ravaged by disease falter economically and their families fall apart which creates tremendous social and economic upheaval.

Humanitarian risk, the risk of disease spread and nation and economic security, these are all powerful arguments for members of Congress and their counterparts in Europe, Asia, Australia and other countries, to take a serious look at this issue.

But Congress and other legislatures will not only be asking why they should make advanced purchase commitments, but whether the policy will work. Although the idea is relatively novel, we have some indications that it could succeed. With a commitment to purchase 18 million doses, the U.K. spurred investment in development of a meningitis C vaccine in the 1990s. Biodefense has been similarly challenging as a market. And Rick mentioned the work of Bioshield and Bioshield 2, the work that Senator Lieberman is doing.

VaxGen recently agreed to supply 75 million doses of a new anthrax vaccine to the U.S. government. Why? Because there was a guarantee of a purchase at the end of the day.

Moreover, the advanced purchase commitment model that's outlined today was designed through extensive collaboration with industry and nonprofits and great health experts like Rick Klausner and many others who are here today. While much more discussion may be needed, the industry and the Congress needs to look at this as a serious issue.

Finally, lawmakers will demand whether biotech companies are really up to the task, and it's a fair question. After all, it's a big problem. As I said earlier, biotech companies are small businesses. But these small businesses have a long track record of success in this area. They have developed more than 200 drugs and vaccines that have helped more than 800 million people worldwide. These products have powerful impact on multiple sclerosis, rheumatoid arthritis, genetic disorders, heart attacks, strokes, and many other forms of conditions and diseases.

Biotech companies are adept at targeting smaller and difficult markets. They're developing two-thirds of the drugs in development for rare diseases. The bottom line is that I think biotech companies are up to the formidable challenge the advanced purchase commitment creates.

Persuading other countries and ensuring individual purchase commitments are sufficient to I believe attract industry investment, and it's an important next step.

So all of us here today are here together to move forward or look at this more seriously. Many of us at least in our community have seen the miracles of biomedical research and the effect that it can have on kids with cystic fibrosis who are now playing soccer, terminal cancer and disabling diseases in many ways eradicated or tamed.

Today this report and the attendance of this impressive group here today I think sends a powerful message that it's time to bring more of those miracles to the developing world. It's time that we square our shoulders instead of shrugging them, frankly. It's time for us to move forward, and we at the biotechnology industry organizations are anxious to help in meeting that challenge. Thank you. Thanks for letting me be here today.

MS. BIRDSALL: Thank you very much indeed, Scott, for driving home the message that we need to make markets. I loved the squaring one's shoulders instead of shrugging. That's a good one.

Now we hear from Dr. Mark Feinberg. He holds joint appointments as a professor in the departments of medicine and microbiology and immunology at the Emery University School of Medicine. He is also the medical director of the Hope Clinic of the Emery Vaccine Center.

I think we've heard from industry, biotech, we've heard from the nonprofit world, and it would be good to hear directly from someone who is engaged directly in the clinical business and presumably an academic and a scholar. **Dr. Feinberg**?

DR. FEINBERG: Thanks, Nancy. Actually, change is good and I am no longer in the academic realm and speak today as a representative from industry, a transition that I recently undertook in July, and I am currently Vice President of Policy, Public Health and Medical Affairs for Merck Vaccine Division. What I hope to provide today is a perspective of industry and what the potential relationship of the Center for Global Development's efforts might be in terms of helping us do what we really want to do which is use our technologies and our production capacity to achieve the same goal that you have which is to help those in need of new and better vaccines.

Merck is very pleased to participate in this important discussion of new approaches to ensure the availability of needed vaccines. In particular I want to thank Nancy and Ruth Levine for their efforts, along with all of the members of the working group for all the hard work they put in to producing this report.

We believe that the work of the Center for Global Development makes a very positive contribution to the ongoing policy of dialogue about vaccine markets, and we appreciate the opportunity to provide our perspective today.

I can speak on behalf of Merck, but I guess I'm being included here not as a representative of academia, but as a representative of industry, and to the extent that I can speak as a representative of industry, I think it is really important that industry be included in these discussions as a real partner because there are things that are easy for industry to do, industry has tremendous capacity to do certain things, but there are other things that are either difficult or impossible for industry to do. And the more that everybody appreciates what the opportunities and limitations are, I think everyone will be in a better situation to accomplish our ultimate goal, and working together in partnership in new models through pioneering mechanisms such as the ones that have been presented or proposed by the Center for Global Development, maybe we can make a difference in achieving our ultimate goal.

Today in particular I want to applaud the efforts that are going on in this group as well as others that Rick Klausner talked about to focus increased attention on vaccine financing and renewed efforts to stimulate research and development to develop vaccines for diseases that are most prevalent in the poorest regions of the world.

Others will focus their discussions in the relevance of the advanced markets' types of arrangements on early stage developmental products, and I'm going to really focus my attention on how this might impact late-stage proposals. In a few minutes I'll talk about specific Merck programs that are in the later stages of development where the CGD proposal could have a positive impact on facilitating the expedited availability of these vaccines in developing countries.

Everyone is familiar with the global need and I'm not going to concentrate on that today, but what I would like to you about is a bit about how we make decisions about which vaccines to develop and the kinds of things we worry about when we have vaccines that are demonstrably effective in developed countries and we strive to figure out how best to implement them in developing countries.

I think it's important to highlight for everyone in this group something that you're probably aware of that I think probably doesn't get sufficient attention outside of these types of gatherings. The research, development and production of vaccines is only one very small part of the successful implementation of those vaccines. Rick Klausner touched upon this issue earlier in this talk in a very articulate way. He, too, used the example, one of which that I wanted to use, which is hepatitis B. I'll talk a little bit about that.

That is an example of it's not simply having a vaccine that is safe and effective. You need a lot more than that. You need the resources, you need political will, you need recognition that this is a important infectious disease that needs to be prevented, and you need the infrastructure and

capacity to deliver the vaccines in a sustainable way in order to have a successful immunization campaign.

Indeed, because we failed to do this effectively with many vaccines, it's estimated that about 3 million children die each year from diseases for which there are vaccines that are available, and that is a shame and we need to do better than that in the future. We need to do better with the vaccines that are currently available, we need to do better with the vaccines that are currently in late-stage of development, and we need to do more to stimulate the development of new vaccines for important and unmet global infectious diseases.

As we talk about what's needed to stimulate research and development, we also need to make sure that when a vaccine is developed there is adequate infrastructure addressed and that issues of advocacy at the country level and at the global level are paid adequate attention because without this we're not going to be successful at achieving our common goals.

I'll tell you a little bit about Merck's approach to vaccine development. We've been in this activity for decades and decades, and it is really in many ways one of the core programs that people at Merck are often proudest of when they think about why it's important for them to work at Merck and why they feel so good about it. These efforts have made major impact on a number of infectious for which you are very familiar, and we are actively engaged in developmental programs for new vaccines for important unmet global needs.

When we think about what programs to get involved in, there are two major criteria that guide those decisions. One is that it needs to address a significant unmet medical need for which there are many diseases that you're familiar that do so such as malaria, tuberculosis and HIV. But the other important criteria that we take into account is the scientific feasibility and is there a biologically plausible path forward for which one could develop a vaccine that would, according to the criteria that Rick laid out earlier, be a vaccine that could not only be produced in small quantities and to protect small numbers of people but that could actually be scalable, produced in large quantities and delivered to the people who need them. That winnows the options down.

Highlighting this in a couple of specific programs that Merck has developed in the vaccine area, particularly hepatitis B, hemophilus influenza type B vaccine, rotavirus, human papillomavirus vaccine and HPV, I think those messages will become clearer.

Merck introduced the first recombinant hepatitis B vaccine in 1986. That's almost 20 years ago. As Rick highlighted, we still don't have that type of vaccine available to all the people who need it. As a result, it's estimated that there are still about 1 million deaths annually as a result of the

long-term consequences of hepatitis B infection, and there are 10 to 30 million new infections estimated to take place each year.

With the demonstration of plasma derived hepatitis B vaccines could be effective by inducing antibody responses against the surface antigen. That was a very important demonstration, but it was not a scalable process and Merck got very interested in developing and applying recombinant DNA technology to the development of vaccines. And with the advent of the hepatitis B vaccine, a recombinant use derived product, I think a substantial progress and a great precedent was made there.

Yet as Rick highlighted, we still have so much more work to do. I think there are a lot of efforts taking place with the support of the Gates Foundation, the Global Alliance of Vaccine and Immunization that we'll hopefully change that, but still it's more than simply having a vaccine in the bottle.

With respect to hemophilus influenza type vaccine, there was also an important unmet medical need. It's estimated that hemophilus influenza type B infections cause at least 3 million cases of serious disease around the world and between 500 and 700,000 deaths each year. It is a major cause of meningitis and pneumonia that are fatal and quite serious in other cases in children around the world. Yet this vaccine is still not available to all the children who need it.

Merck was one of the pioneers of this technology that made more effective hemophilus--

[End tape 1, side A. Begin tape 1, side B.]

DR. FEINBERG: [In progress] --try to solve some of the implementation's needs as well as provide funding for that vaccine, then more children will be able to benefit.

Turning now to a number of the vaccines in development, I think you'll see where we are with a number of these promising new products. But I think you'll also appreciate the challenges we face and leave it up to you as partners and to the people who make suggestions to us positively about how we can go forward with the capacity and resources we have to partner with others to make sure that these vaccines do attain the important global reach that they need.

Importantly, I'm going to talk about rotavirus, human papillomavirus and our HIV/AIDS vaccine development program.

As many of you are probably aware, rotavirus is a significant cause of gastroenteritis and diarrhea which in developed countries is a serious problem, but in developing countries exacts a very significant toll on young infants, and approximately 500,000 kids are estimated to die in poor countries each year from rotavirus associated gastroenteritis.

There was a scientific path forward. It had been shown that rotavirus vaccines were possible, but unfortunately the earlier generations

were either not sufficiently effective or not sufficiently safe and using newer technologies to make reassortment viruses, Merck pioneered the development of a bovine reassortment virus that protects against five different rotavirus strains that are circulating worldwide.

With the recognition that some earlier generation rotavirus vaccines had some safety concerns, Merck invested in mounting what is likely one of the largest clinical vaccine programs that has ever been undertaken involving 70,000 children in 11 countries around the world. Again, this is an important disease both in developed and developing countries, but I think many people earlier on were worried that there may not be a rotavirus vaccine because there wasn't not so much a clear scientific path forward, there wasn't a clear path forward, but hopefully those concerns have now been ameliorated. This 70,000 infant trial has recently been completed and we're encouraged by the safety and efficacy date of this vaccine and now our challenge is to figure out how to get it to the kids around the world who need it. It's a complicated vaccine, it's an effective vaccine, it's an important vaccine and we want to do all we can to help in partnership with others to make it available.

Turning now to the human papillomavirus vaccine, I think many of you are aware that that human papillomavirus is the cause of cervical cancer and this infection is resulting in about 500,000 cases of cervical cancer worldwide, and about 233 deaths are due to cervical cancer, almost all of which or at least many of which are in the developing world where there are not screening methodologies in place to protect women against the development of cervical cancer.

With respect to a scientific path forward on the background of a serious medical need in partnership with others developed the technology of virus-like particles, again a yeast-based recombinant system, to develop vaccine candidates. And in recent proof of concept studies where one was asking what would be the protective mechanism that one might need in a vaccine, what type of immune response would you need to induce by a vaccine to protect against cervical cancer, there was a very clear demonstration that virus-like particles eliciting antibody responses could be impressively protective against HPV infection. As many of you may hear in the news today, the results of a large phase two study were announced where this vaccine, quadrivalent vaccine against four major HPV types was shown to be 90 percent effective at reducing the incidence of persistent infection with these virus and 100 percent effective at preventing precancerous lesions, and that's just a very startlingly encouraging result.

Yet how do we go about getting that to all the people around the world who need it? Clearly, we can't do it on our own. We need partners. We need a good idea about what the market would be and what production capacity is necessary.

One of the major focuses of the Center for Global Development's report was the idea about stimulating early stage products in the development vaccines for important infectious diseases such as malaria, tuberculosis and HIV. Merck has been actively engaged using its own resources in HIV vaccine development since the mid-1980s, essentially coincident with recognition of the viral etiology of this disease being HIV. We continue to be devoted to the development of an effective vaccine for global use.

This activity builds on the backdrop of Merck's efforts in developing effective antiretroviral therapy, again focusing on a significant unmet medical need, as well as a path forward with respect to technology. I think many of you in the room will probably remember in the early '90s there was a lot of uncertainty about whether we ever would have effective antiretroviral therapy for HIV infection. It may just be an untreatable disease, and that changed dramatically with very productive insights emerging from basic science discoveries, a number of discovering at Merck research laboratories, and the development of new paradigms of combination antiretroviral treatment that totally changed that scenario in enabling people infected with HIV to live much longer, very productive lives.

Then the challenge became one that you're all very familiar with, how do you get this effective, complicated antiretroviral therapy to all the people around the world who need it, and that's something that is requiring significant resources. It's fortunately garnering significant attention, but you need partnership models to make that available.

Merck has dedicated itself to trying to do its best to make these drugs more widely available and practices no profit pricing in developing countries. We're particularly pleased of our activities in collaboration with the Gates Foundation to provide treatment to the people of Botswana as part of the African Comprehensive HIV/AIDS Partnership.

As we look at HIV vaccine development though, clearly the scientific challenges are major, but our investment in this and our interest in this remains strong. Last December Merck initiated in collaborated with the HIV Vaccine Trials Network a so-called proof of concept study to test the idea of cell mediated immune responses to HIV prior to infection would either prevent the infection or favorably alter the postinfection outcome. That idea if the central idea in the field of HIV vaccine research now, and it is essentially important both for Merck and for everyone else to know whether that idea is valid or not. Hopefully this proof of concept study of Merck's trivalent MRK 5 adenovirus will provide that answer, and that answer is anticipated in late 2007 or early 2008.

We sincerely hope that that study will give us the desired result, that it will have a big impact on either preventing infection or favorably postinfection outcome. However, we wonder what will happen if that study is strongly positive because the world is not prepared to implement an AIDS

vaccine right now and it would require significant investment on many people's part to make that possible. We definitely hope that we will have that challenge to work with you in solving.

So with respect to how we propose to try to get these late-stage products into the countries that need them, we seek to work with others to be more effective than we have been previously. We seek to partner with others such as GAVI/The Vaccine Fund and various other entities of which you are familiar. As we go about doing this, we're planning on pursuing a staged introduction approach would be based on the availability of a significant body of epidemiologic and clinical data in the countries being considered, the adequate resources and political will within those countries, and the development of a clearly articulated plan.

We would imagine this approach would call for an initial vaccine introduction in the countries that meet these criteria, namely, sufficient political will and adequate basic biological and medical demonstration of a medical need and likelihood that the vaccine would work, and we would work with partners to initiate the requisite studies, clinical evaluation, disease education and advocacy in the countries to promote introduction in the next phase.

Merck's contribution to this partnership would include providing the vaccine, conducting epidemiological and clinical studies, supporting advocacy and disease-awareness programs, meeting local regulatory requirements, and practicing differential pricing.

With respect to rotavirus, we're working with GAVI and the Rotavirus Vaccine Program to try to accelerate introduction of the vaccine into the areas of the world that need it. We're working to identify other partners to develop implementation of the HPV vaccine, and hopefully we'll be fortunate enough to have the challenge of doing so with an HIV vaccine as well.

With respect to what I've talked about today, I'd like to close with some thoughts. Namely, vaccine introduction is going to require a significant commitment of resources to address a wide array of important needs. It's going to require the partnership of donors, developed and developing world governments, industry, and international organizations, and I think these organizations will have to find ways of working together in more extensive and more effective ways than we have previously.

We welcome the development of initiatives like the Center for Global Development's advanced market proposals because in particular for vaccines like rotavirus and HPV, this type of initiative would definitely help us plan appropriate manufacturing capacity to serve global needs. And should we ultimately have an HIV vaccine, an advance purchase vaccine guarantee would help implement that worldwide as well.

In closing, we appreciate the opportunity to participate in this important policy dialogue, we look forward to a continued dialogue in the

future, and hopefully we will accomplish the goal laid out in the subtitle of this report, translating ideas into action. Thank you very much.

MS. BIRDSALL: Thank you very much, Mark. I think it's a happy accident that I made such an embarrassing mistake for several reasons. One is that I was thinking that our three keynote speakers representing the public sector, the public sector and the nonprofit sector constitute or reflect what is a terrific asset of this country that I wish the developing world had which is that thick web of interaction and transfer of people that carries that interaction and make ideas that get turned into action.

I want to thank all of the speakers. I do apologize to Mark and to Merck, but it gives me a second reason to say it was a happy accident which is that as you step down, I think that's next, and we enter the next stage of today's event which is the presentation of the working group report, I have the honor and the privilege to introduce Ruth Levine who knew very well where Mark came from, and John Hurvitz.

Let me say a word about Ruth as you come up, Ruth. Ruth is a Senior Fellow at the Center for Global Development. She is the director of programs for us, and she is the head of the Policy Research Network of the center. I think to say she's the head of it is to minimize too much her role.

She is the inventor and the architect of the idea of the Policy Research Network in Global Health and she has been already in three short years the key contributor at the center to our success in generating what Rick called actionable, evidence-based ideas. She is wonderfully stubborn about insisting that we ask the right questions, and when we come up with good ideas, we work hard even thinking about what the right questions are on ensuring that those ideas are actionable and can make a difference for people.

Ruth, you have the floor, and you'll introduce John, I hope.

MS. LEVINE: Thank you very much, and I want to thank Nancy as well as the speakers who preceded me partly because they did such a fantastic job of motivating this discussion and said such nice things about our work, and partly because they covered about 50 percent of what I was going to say, so we can get right to the meat of things.

Before starting, I want to say what we're going to do is I'm going to in representation of the working group's effort and my co-chairs, Alice Albright and Michael Kremer, I'm going to present the background and start of the content of the working group report. Then I'm going to turn it over to John Hurvitz from Covington & Burling to continue and get into a few of the details because it is actually a case where the devil is in the details.

I'm going to introduce John before I start and then he'll follow me. John Hurvitz participated in this project as our main legal counsel and he is the co-chair of Covington's Life Science Industry Group and chair of its Technology Transactions Practice. He is a partner at the firm. He is also an

adjunct professor at Georgetown Law School and teaches FDA law or something similar to that.

It's been a tremendous pleasure to work with John on this. He has devoted untold hours. I certainly hope he's not keep track of the number of hours he's devoted to this project. As I say, it's been a tremendous privilege and pleasure to work with him, and I think I'm the only person in Washington who is very happy when I hear somebody say, your lawyer is on the phone.

What I'm going to cover very briefly again because it's been highlighted before is the toll of infectious diseases in the developing world, the barriers that currently exist to more and better immunization, the current solutions, many of which are working, and a possible new solution to fill a hole in the landscape of providing the right incentives for more and better immunization. Then John will take over around that point and talk about what the contractual arrangements actually could look like.

Before starting I want to make sure everybody is on the same page on the vocabulary. When we talk about near-term vaccines, we're talking about vaccines that are either very close to licensure or have perhaps just been licensed where much of the research and development, the basic science, has already been done as well as most of the clinical trials.

When we talk about long-term vaccines, we're talking about products that are several years, perhaps many years, away from licensure. They face important scientific hurdles either in the basic science or in the early clinical studies and where the expensive and risky R&D is very much underway.

When we talked about a treatment, it's sort of a funny term, but it refers to a full course of vaccines that are required to achieve immunity. So you can have a three-dose treatment. Push incentives as has been noted before is direct investment in R&D. Pull is some kind of a reward upon development of a product.

When we talk about an advance market commitment which is the proposal that we have on the table, we are not taking about a quantity guarantee. I think it's easy to get that a bit confused.

You've already heard today about the toll that infectious disease takes on the developing world. Vaccines in use today could address about 3 million of those deaths and prevent them. Measles, hepatitis B, HIB and so forth. So there is clearly a challenge on delivering products that currently exist and in most cases are not very costly.

Then there are vaccines that are on the horizon, either very recently having been licensed or close to licensure for rotavirus disease and pneumococcal disease.

Then there are vaccines far in the distance where there is currently significant but not enough R&D being done for HIV, malaria and TB, and that accounts for as was highlighted earlier more than 6 million deaths annually.

The challenge before us is to see how to achieve better health in the developing world through faster development of new vaccines and more access to existing and newer vaccines. The constraints as others have highlighted are that developing country markets are very small relative to the industrialized world, government purchasing can be unpredictable, that prices tend to driven quite low, and I'll talk about that in a moment, and the disease burden between the industrialized world and the developing world is diverging.

I believe it was Scott who mentioned the large differential between per capita health spending in the industrialized world and in the least-developed countries. $17 per capita is under no system enough to provide the health products and services that are required to achieve even a modest level of good health.

If we look at the current markets for pharmaceutical products, a very similar pattern arises. So what you have on the highest bar is the total revenues for all pharmaceutical products globally on an annual basis. Of that, a very small percentage is for vaccines, and that's globally. Overall, vaccines are a small part of the total pharmaceutical business, and of vaccines, the vaccines that are purchased for the developing world are a vanishingly small part of the revenue streams even though they account for something like 50 percent of the total volume of vaccines.

That's because the vaccines that are currently used in the developing world for the most part are very inexpensive. They are off-patent vaccines for the most part, many produced by emerging suppliers in countries like India, and they are purchased largely through a pulled procurement process in which the procurer has a tremendous amount of market advantage in getting prices down to the lowest possible level.

I've given you a picture of the relative sizes of the markets between the industrialized world and the developing world. Now I'll give you a picture of the diverging causes of death.

As you can see and know from your experience, communicable diseases represent the lion's share of the disease burden in the developing world, whereas noncommunicable diseases represent the vast majority of causes of death in the industrialized world. The consequence of this is that the markets that are pulling drug and vaccine development are really from the industrialized world and they're unlikely to pull products that are of value to the developing countries.

In the past, developing countries benefited by using vaccines that were developed first for rich countries, for your children and mine, and those countries we paid relatively high prices at first, offsetting the initial risks and R&D costs. Then they were made available partly by being off patent and partly through scale-up manufacturing to the least-developed countries. That's a model that is unlikely to be able to work in the future. If you just hold

malaria in your mind as an example, you can see why. There is not that initial market in the industrialized world.

Let's look at how pharmaceutical R&D is paid for. I want you to take these numbers as really quite rough. There are a lot of difficulties in obtaining data about the total R&D costs and some differences in definitions that go into the different estimates.

What's shown in the top pie chart is how the different sources of financing shape up for total R&D for the pharmaceutical business. The single largest source is private spending. However, government spending is of course a very important part of total spending on R&D through NIH and through other direct funding of research. The top pie chart is the picture for total R&D which is mostly the industrialized world.

For R&D for products that are specifically targeted at developing country diseases, R&D spending first of all represents as you heard earlier only about 7 to 10 percent of the total despite the disproportionate disease burden. The sources of financing are very, very different with the vast majority of financing coming through government for direct support of R&D. The other captures foundations, universities and other nonprofit sources of funds.

Then you can see that there is a little slice of private investment. We've heard about some of that today, but it is relative to the other sources of financing a relatively small part at the moment. It's a very different picture for who is funding the R&D the industrialized world's products, and who's funding the R&D for the developing world at the moment.

Just to summarize, the problem we see, low investment in research and development relative to the social importance, potentially missed opportunities for innovation of the private sector if the pharmaceutical industry is not fully engaged in harnessing its innovative potential to solve the problems of the developing world, and as has been pointed out earlier, long lag times before the introduction and scale-up of life-saving products that have been developed for the industrialized world. I think there was a reference to 20 years. It can be 10, 15 to 20 years in some cases.

There are several solutions, some of which have been talked about today. One is buying products today. Buying the existing products through the Global Alliance for Vaccines and Innovation and it funding arm the Vaccine Fund, creates a more visible market for existing products and strengthens delivery systems. In the consultations we did in this working group, a strong signal that came back from industry was the importance of GAVI and the Vaccine Fund in creating a signal that, yes, there is something out there that will purchase at least the existing vaccines.

Another solution is preparation for future products through the advanced development and introduction plans, work on better forecasting of

demand, creation of markets, and getting information out to developing country decision makers about the value of vaccines.

Finally, a solution that's currently in place is investing public resources in R&D, and that also includes foundation resources through product development, public-private partnerships, we'll hear a little bit about that from panel members later, and through collaborative research arrangements such as the HIV Vaccine Enterprise Program.

One thing that's missing in all this is a market for future products. Taking that into consideration, in March 2003 the Center for Global Development convened a working group to look at this problem, sponsored by a grant from the Bill & Melinda Gates Foundation. We started very much with Michael Kremer's previous work in mind and asked the question, could a advanced commitment for a future vaccine product work? When we took the question, could, we meant could it work in the real world, are there particular arrangements that could be made that are legal that would permit this to happen?

Then the other dimension of "could" is could it actually stimulate additional private investment in R&D, more R&D, and potentially a faster movement toward newer vaccines.

We pulled together individuals with expertise on the industry side, public policy, legal and regulatory issues, public health, economics and others. We really strove to try to identify a practical solution and in the process consulted widely with many, many people in this room. So now you see that all those conversations were not for naught.

Before going on to the assumptions, we started with recognize the work of Gargey Gauche (ph) who worked on this project with me at the Center for Global Development for about a year, and more recently, Owen Barter (ph) has joined our team and has been instrumental in completing this work.

The assumptions that we started with are pretty basic. One is that there is a production function for research and development. More money for research and development would lead to faster progress on average, that firms allocate capital based on some kind of calculation of risk and reward, that firms face major opportunity costs that affect R&D investment decisions. When they're trying to figure out how to allocate their capital, they think we could spend it in one way or we could spend it in another, and part of what goes into that calculation is the risk and reward. On the reward side, it has to do with what the size of the market is, among other factors.

We also made the assumption which I think can be backed up empirically that to get to a situation where you actually have a product that can be manufactured at scale and delivered, you need industry engagement, that this cannot be all university-based for the full life of any project. We asked ourselves a question, can these market incentives be used to promote an

accelerated development path, quality, low cost of production, and rapid scale-up?

What's in the report is a description of an arrangement whereby a sponsor or a set of sponsors would make an ex ante specification of the vaccine product that that sponsor would be willing to buy if and when it were developed. The specification has to do with how effective the vaccine is, how long the duration of protection, what the target population is, and what the vaccine presentation is.

Sponsors would make a legally binding commitment to purchase that product if and when it's developed in the future. They would do so by underwriting a guaranteed price with the price specified in advance for a maximum number of treatments. So if a set of developing countries demanded 100 million treatments, the developing countries would pay a small, rather nominal amount per treatment that would be topped up by the sponsors, again, for treatment. These products could be procured through the normal channels that they currently are; that is, typically through UNICEF.

The combination of price and maximum quantity of treatments would provide an adequate return to suppliers that would be adequate to get their attention, taking into consideration the opportunity cost of capital, as well as the alternative markets they might have for a product that could be sold in markets other than the least-developed countries.

Part of the deal would be that the suppliers would then agree to provide the product after the maximum number of treatments had been purchased at the relatively high price, the suppliers would promise to provide the product at an affordable price after that point, and that would be after the cost of the R&D had been captured.

Let me just walk through briefly an illustrative example for a malaria vaccine which is in fact the one that we looked at in the working group report merely as an example to discipline the working group's thinking. This is not in any way to suggest that these are exactly the specifications should look. We didn't undertake that detailed a process that would be required if there were a real sponsor in the room.

With respect to technical specifications, they might look something like this, that the product would have to be targeted against falciparum which is the major cause of death; that it would have to achieve something like a 50 percent efficacy level against clinical malaria. That's a specification that in the current context might be seen as actually quite ambitious. The main point there is that that efficacy level would have to be higher than the competing ways that disease would be prevented, and it should be set quite high because if you're promising a significant reward, you want to make sure that the benefits achieved are at least equal to that reward. Perhaps a 2-year duration of protection, and something about the presentation of the product as well.

Total market value, again, keeping opportunity costs in mind, we set the total market size at 3 billion in net present value 2004 dollars. What is that 3 billion? First of all, it's a number that should be validated using lots of different data sources and so forth. We used one particular source of data, and there are others that could be mobilized to do some reanalysis.

The basic concept behind this is that that is equal to the average returns that pharmaceutical companies obtain for the revenues the average new chemical entity in developed country markets. So this is in concept the opportunity cost or it takes into account the opportunity cost.

As I said before, sponsors would underwrite a specific price. We used in this illustrative example $15 per treatment. If it's a three-dose treatment, then it would be $5 a dose, and I want to say that that is higher I think than any product that is currently being sold in the developing world, a vaccine product through government channels, but I stand to be corrected on that.

The price guarantee applies as I said before to a maximum number of treatments. What we have as an illustration is the first 200 million treatments, and the price combined with that quantity gives the total reward to the firm or firms who are eligible to receive the reward.

In the example that we have, the treatments sold in eligible countries, we took vaccine fund eligible countries as the standard. In return, the long-term price that would be guaranteed would be $1 per treatment. This again could vary, but the idea is that it would be ex ante and that it would reflect some level of affordability for the recipient countries over the long-term.

When you work through this particular example using these parameters, what you come out with is an extremely cost-effective bargain for the sponsors, something like $15 per disability-adjusted life year under those circumstances because malaria is such a devastating disease. Even though we're looking at relatively costly products, when you take into account the impact on health outcomes along with the lower price in the end, it can be a very cost-effective intervention from the sponsor's perspective.

An important feature of this is that it's not a winner-take-all arrangement. It is not that it's restricted to the first supplier who comes to a sponsor with a product that meets the specifications. If a superior product is developed later, then a share of the reward would go to that supplier based on the from the developing countries.

I think John will talk in a moment about the Independent Adjudication Committee or some independent structure that would be required to be the judge of whether a particular vaccine met the specifications and was eligible for the reward.

John, I think I'm going to turn it over to you now.

MR. HURVITZ: Thank you, Ruth. Thank you everybody for coming.

This entire project and process has been extremely gratifying for me. It's not often, in fact it's often a challenge, for a deal lawyer or business lawyer to get their clients to actually read the contract, and to have 200 people showing to actually hear you talk about a contract is pretty much mind-blowing for me.

The opportunity that this project has presented and the promise that it shows for me, somebody who day in and day out is dealing with commercial situations in the pharmaceutical industry, from my perspective is just phenomenal and to be a part of it has been tremendously rewarding.

What we did and what I'm going to talk about in a minute is that we essentially took basic contract and business principles and we creatively brought those to bear on the problem that's been presented today, how to create a binding, enforceable agreement that donors would put out there that would stimulate the behavior of industry.

What we did involved a lot of complicated and thorough analysis, but the result, the contracts, are actually very, very simple and straightforward, and I think that's really the beauty of the system. So first I thought what I would do is walk you through a time line of how this would play out in practice.

The first thing that would happen is you'd have the announcement of the framework agreement. That essentially sets forth the rules of the game, it establishes as Ruth mentioned this Independent Adjudication Committee, it would set out the product specifications, what somebody needed to achieve in order to win, and it would set out the guarantee, the prize or the market that is being established by this process.

At that point, then companies would sign on. When companies sign on, it would make it a binding contract. The beauty of this is that what you have at the outset is a bilateral contract that is binding on the donors. Donors do not need to put forth money at that point. They don't need to escrow funds. They don't need to obtain a letter of credit. What we have is a contract, something that's very familiar in industry and business practice, something that be enforceable in the courts if the donors fail to deliver. But what it means is that you don't have to invest money today. You obviously have to have adequate resources in the future when a qualifying product is tendered, but you do not have to have the money set aside today which means that those funds can be used for immediate opportunities. They can be used for push opportunities, they can be used to fund the consortia that we talked about. They can be used for all measure of other more immediate, near-term goals. It complements other existing mechanisms, it doesn't compete with those mechanisms.

Under the framework agreement, the companies that sign on, the developers, have very, very limited obligations. They provide periodic reports. The purpose of that is so that the sponsors know what's going on and know that this is working. It provides an opportunity to measure the success, but that's about it.

The developers, the manufacturers, aren't committing to actually develop a vaccine. Hopefully they will. That's why they signed on. They have an interest. It enables them to participate in the guarantee agreement later on in the market that we talked about before, but it doesn't obligate them to develop a product. If they do not develop a product, they're not in breech of the contract. But if they do develop a product, and that gets to the next step in this process, then they have the right to sign on to the guarantee agreement, an agreement that's attached to the framework agreement, but they don't have the obligation. They don't have to participate even after signing on to the framework agreement, but they have the right to do so.

The difference for the donors is that they have the obligation. The framework agreement establishes on the donors the obligation to deliver the money if somebody delivers a qualifying vaccine, and that is an enforceable contractual obligation, and the framework agreement can in addition to being enforced in the normal way that normal contracts are enforced, can include penalties if the funders were to fail to satisfy their obligations.

As I said, the guarantee agreement steps in. That puts in place the price guarantee. It requires that the manufacturers have adequate capacity to meet their obligations under that contract. Then the vaccines would be delivered. There would be adverse event reporting. There would be monitoring to make sure that the product that's tendered continues to meet the obligations of the contract, the framework agreement, that it's manufactured in an appropriate facility, in a qualified facility.

Then there is the possibility, as Ruth mentioned, that you could have superior vaccines come along. One of the beauties of this, and we'll talk about it in a second, is that you're not locked in to the first product that comes along. New products can come along. If they're better, they can participate as well in that guarantee. So it reflects the actual market just like it would in the developing world. New products come along, consumers make decisions as to whether they want to use new products or old products. This has that same feature.

Then finally, as I mentioned, when the commitment is exhausted, the manufacturers have an ongoing obligation to continue to supply the product, and they have to do so at an affordable price. So they will no longer get the hypothetical $15 a dose, but they will get something smaller, lower, a sustainable price that the countries could actually afford going forward over time, and we'll talk about that in a little more detail in a second.

So as I said, there are a lot of things you could say about this contract structure. A lot of thought has gone into it by a lot of people, but for today's purposes, we'll just distill a few high-level points to make sure we all understand the basics.

As I said before, some of the critical components from the donor's perspective is they have to provide an approved vaccine. Their framework agreement will set forth technical specifications, usability requirements, approval requirements, and that's what the developers, the manufacturers, the industry, has to do in order to have a right to participate in the market.

In order for the sale of that product to trigger a payment obligation by the donors, it has to be a qualified sale. It has to be sold to an eligible country for use in an eligible country, and there has to be a reasonable expectation that that product will actually be used in that country. So if the market demand in a country is for a million doses and you're selling 2 million doses in a year, you're not going to get paid for 2 million doses, you're going to get paid for 1 million doses. And there has to be, as I said, adequate capacity.

The manufacturers, one of the commitments that they have, is that they have to meet the demand in all eligible countries. They cannot pick and choose countries. They have to be able to meet the supply during the guarantee period and going forward.

As we talked about before, what we're creating is a market. We're not creating a prize. We're not creating a commitment to buy a quantity of product, as Ruth said. What we've set in place is effectively a copayment mechanism similar to what we experience when we go to our local pharmacy to buy a product. We go in and we pay the $10 copay and somebody else pays the additional $50 or $30 that the drug actually costs.

In this situation, the UNICEF mechanism or whatever mechanism is used, would purchase the drug as long as a minimum copayment amount was made, the dollar, then the donors would come in and step up that amount to $14 in a direct payment to the industry. That would be separate from the chain of commerce.

This system as I said before provides incentives for innovation because you're not locked into buying the first product. The market actually decides what products will be purchased by what it actually buys, and that determines how the donor's commitment will be used. It allows for less-exhaustive specifications, so it lowers the risk for donors.

With an early stage product opportunity, we don't know with certainty what, for example, malaria is going to look like in 10 years or 5 years, so you'll set the specifications as best you can. But it may be that you haven't thought of something or it may be that circumstances will change. By allowing the market to be a second test, the fact that a country has to actually buy the product and somebody, whether it's the country or a donor, has to--

[End side B, tape 1.]

[Start side A, tape 2.]

MR. HURVITZ [continuing]: --but it also encourages the developers, the manufacturers, to produce the best possible product, because they're not guaranteed that if they just get right above the wire, they're going to get the whole market.

They're going to have to compete. There may be follow-on products that are better. So they have an incentive, that when they come to market they should come to market with the best possible product, so that they can take advantage of that pool of money, that market, as quickly as possible, before others come along and compete with them for that, if that happens.

And probably most importantly is it allowed the developing companies to choose, it lets them select what products they want to use, and then the advanced markets mechanism essentially allows that to happen, it helps fund it and helps subsidize it.

So the important message is that it's an advanced market commitment. It's not a purchase commitment. It's creating a market, in effect.

Now we talked about--the graphics got a little screwy on this graph but hopefully you can sort of get the picture of what's going on.

The 3 billion box there should actually be over to the left, and this is just reflecting the two-stage pricing structure that is inherent in this contract.

What happens at the outset is that the market, as we talked about here, is the $3 billion market, the agreement to buy 200 million doses, treatments, at $15 a treatment. And during that period of time, the donors will step in and will bring up the price to the $15. After that, it drops down to the long-run price which, in theory, would be slightly above the marginal cost of production.

Now the important thing here to keep in mind is that the donors are buying two things in this contract.

You're buying the acceleration of the development and access to, acceleration of access to new vaccines. That's one thing. That's what we spend a lot of time talking about. But you're also buying sustainability. You're buying a long-term price. So you're not paying twice. It's not like you're paying today, you push and then you pay again, and then you pay more later. You keep paying and paying.

The theory behind this is that you pay the 3 billion and what you're buying through an enforceable contract is a commitment by the manufacturers to continue to supply the product at an affordable, sustainable price, that the countries could afford, going forward.

The benefits of this two-stage pricing, as I said before, it incentivizes the developers to get there first so they can take advantage of it quickly. It incentivizes them to get it right the first time.

It leads to affordable pricing, overall, as I said. For the manufacturers, it maximizes the NPV [ph] of the commitment because more money's available up front, increasing the present value of that investment, and it rewards the first developer but doesn't stunt, doesn't chill future developers from coming on board. So it doesn't chill innovation.

Now probably the most important part of this, and the biggest challenge in putting an advanced market contract in place, is that you need to have a binding contract on the donors but you need to have some degree of flexibility because you don't know what the future's going to bear.

And the next couple of slides are really just designed to illustrate some of the mechanisms that were put into the contracts to ensure that we have flexibility.

And the most critical aspect of that is this independent adjudication committee. The key with this committee is that you have to have it be credible to industry, it has to be somebody that industry views as being competent to make important decisions, but also independent.

And the theory in this is that the IAC would basically have final say in most decisions. A few exceptions which we'll talk about in a second, but generally the IAC is the final arbiter.

So this gives the flexibility, it allows the framework agreement to deal with future uncertainty. So the IAC would approve qualifying vaccines. We contemplated that the IAC could rely on outside experts. It could utilize the WHO prequalification process. It could utilize government approval processes in countries. So it wouldn't have to do everything itself.

It would approve the superior vaccines as we talked about. Importantly, it would grant waivers, and the IAC would have the right to lower the bar. So it can't raise the bar unilaterally but it can lower the bar, so that if it turns out that the bar was set too high and there's a very promising vaccine that everyone agrees would be really useful, it could set the standard lower and let somebody come in with that vaccine.

And the IAC would also be available in a consultative fashion, the same way today companies go before the FDA, for example, to talk to them about products that they have in the pipeline, so that they can learn--you know, they want to know what the people who are responsible for approving are thinking.

They want to design their trials, we want to design your regulatory approvals in a way that the people who are going to make the final decision want it to look, the way they would like it to look.

There's also exit provisions. So what if something goes drastically wrong? And there are two of those built in. One's a force majeure provision. If something dramatically changes. You start with a vaccine for malaria and it turns out malaria's eradicated through some other means, through sanitation, through insecticides, and it's no longer the problem it is today.

Well, in that circumstance, there could be built into here an exit provision. The IAC would make that decision in the first instance but it would be subject to judicial review, unlike other decisions. You could appeal it and the framework agreement would articulate the standard that we started with, so there'd be a basis for that appeal.

In addition, there's a sunset provision. I mentioned at the outset, that there'd be reporting, over time. Well, the sunset provision would say if nothing's happening, if, in ten years, there's no a product that's even in Phase I trial, then the IAC could pack up and go away. We could fold up this contract, say it didn't work and move on to something else, move on to another disease.

The one thing I'd like to just mention before I turn it back to Ruth is about late-stage opportunities.

Most of what I talked about so far dealt with these early-stage opportunities. This model also applies with late-stage opportunities and the panel later will talk about this in a little more detail.

Some people may say, well why do you need it? Market uncertainty still will affect investment decisions. I think we heard that very credibly this morning from the industry people. Whether there's going to be an investment in necessary process scale-up for manufacturing, whether there's going to be an investment in capacity, the specifications or the presentations of the product, whether they'll be suitable for the developing world.

The development process. How quickly development will happen for these diseases, and also the approval process.

But with late-stage opportunities you have a better idea of what the product is and you have a better idea of who the players are, and in those circumstances you have the possibility to negotiate specific bilateral agreement, just like you do in normal business dealings, where the parties can get together and figure out what each needs to move the ball over the line.

So, with that, I'll turn it back over to Ruth for final comments. Thank you.

MS. LEVINE: I just want to say that I hope that this is the start of an interesting conversation and we're about to turn to one now with the panel participants.

MR. MacDONALD: Thanks very much, Ruth and John, for a very stimulating presentation. While our panelists, if the panelists would please take your seats here on the stage, your assigned seat, so that I'm able to introduce you properly.

I also want to invite you to take your coat off. If anybody is as warm as I am--we've tried to reduce the temperature in here but it's about the best we're able to do. And also to say we have not only an extremely distinguished panel but a very knowledge gathering here generally, and I know that many of you will have questions and comments.

My colleagues will be coming around the room and passing out three by five cards, at the end of the panel which I'm going to discipline very harshly, to make sure that we give everybody a chance to speak. They will come around and collect your questions.

Owen Barter [ph], who's both a member of the working group, lead author of the report, and the author of CGD's new blog, vaccinesfordevelopment, and one of my colleagues will then sort those questions and hand them to me and I'll read them out.

Every question will get answered, if not here today, then through Owen's blog. He has promised to undertake getting answers, and that would include not only from our distinguished panelists but also from the keynote speakers and from the presenters today.

With that, it's my pleasure to introduce our panel. You have their biographies in front of you, so I'm not going to waste their time and yours, telling you about their achievements, but I will say a word about the organizations that they are, in most cases heading, or very actively involved in the leadership of.

Alice Albright, who many of you know, is both a co-chair of the working group and is also the chief financial officer of the Vaccine Fund which works to ensure that every child, everywhere, has equal access to life-saving vaccines.

Rudi Daems is the executive director, policy and corporate affairs, for Chiron, a biotech company in the business of biopharmaceuticals, vaccines, and blood testing.

Michael Kremer, known to many of you, is a professor at Harvard, senior fellow at Brookings, and we're very proud to say a nonresident fellow at the Center for Global Development.

He is the author of Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases, a co-chair of the working

group, and a lead author of the report that you have in your hand, together with Ruth Levine and Owen Barter.

Orin Levine, to the left of Michael, is the executive director of PneumoADIP, and the full name of that organization describes exactly what it does, pneumococcus accelerated development introduction plan. For the likes of me, it means that they try to get vaccines for respiratory diseases to poor children in developing countries.

And finally, I'd like to introduce and welcome Melinda Moree, the director of the Malaria Vaccine Initiative. The MVI worked to accelerate the development of a malaria vaccine and ensure its availability and accessibility in the developing world.

Rudi, the first question for you. To my mind there's really only one question about this whole proposal and I'd like your opinion on this.

Would an advanced market commitment of the kind that we have heard described today give Chiron and its competitors in the biotech industry enough incentive to significantly increase investment in R&D for vaccines against diseases such as HIV, TV, and malaria.

MR. DAEMS: Yeah; thank you for the question. Well, first off, let me tell you that I'm a great proponent for this AMC proposal, the advanced market commitment.

Actually, I also had an opportunity to discuss this with the CEOs of the six major vaccine research based vaccine manufacturers at our meeting last week in New York in preparation of the upcoming GAVI board meeting.

Now while there is some education to be done at CEO level, I believe you can safely say that this probably is the proposal, at least in my opinion, that we've been waiting for for quite some time.

It tackles the issue right on. It also is a proposal that I find, one of the very few I've seen so far, over the last couple of years, that truly understands industry, and by that I mean industry wasn't a part of the working group, which is appropriate, but definitely, it's clear from the proposal, that people have an in-depth knowledge gained through consultation with industry.

And therefore I give it a very high chance to be adopted by industry and really do what it wanted to do, and that this made the private sector work for you to achieve your public health goals.

Now to basically highlight to you what, on your question on how the AMC will incentive industry in conducting R&D for vaccines for diseases such as HIV, TV and malaria, let me briefly tell you what AMC will do for industry in making its investment decisions.

Basically, what I'm saying over here is always, invariably, in whatever type of product we go into, in terms of product development,

you've got to make a tradeoff between the investment and the risk you're going to take, and basically there are two sets of risk factors.

MR. MacDONALD: You're going to have to make them really quick because you got first mover advantage. I was going to give everybody one minute and I forgot to say it. So I'm going to let you go over.

MR. DAEMS: Let me tell you then, short, the three risks factors, there are subsets, but the three risk factors are technical in nature, market and financial, and without going into further detail, it is the second one that is blocking us in these therapeutic areas. It is a clear case of market failure; not industry failure. Actually, nobody's failure. One of the highlights here was that yes, the poorest countries only have $17 to spend on an annual basis per person on total health care.

Whatever you're going to manufacture, knowing that the average price, of the average price of any vaccine being developed, or medicine, is about 100 million U.S. dollars, the price will never be low enough for these people to buy.

So if the AMC addresses the major issue being a market failure, I believe we have found a solution to our problem.

MR. MacDONALD: Rudi, thank you very much and I'm sure that's music to the ears of many people in this room.

Melinda, your organization, the MVI, works to accelerate the development of an effective malaria vaccine. Isn't it the case that a malaria vaccine is already widely understood as crucial and that governments and foundations are already funding the necessary research?

What difference would an advanced market commitment make to a malaria vaccine?

MS. MOREE: Well, you know, for industry, time is money, and so for a profitable vaccine, where a company might make a billion dollars off of it, every month of delay is up to $100 million in lost revenues, and those revenue are lost and they're never recovered again.

For malaria, every month that we delay, 80,000 kids die of malaria, and those lives are lost and they're never to be recovered.

So when you talk to me about speed to market, to me, I think of that not in, you know, time to market, we save this much money, we made this much more money, but I think of it as additional lives saved.

So, for me, any increase in speed, I count it in terms of lives, and I think that this mechanism would be highly effective in getting there.

Just a small part, cause you asked me a two-part question, so I get another 30 seconds, is on the part of isn't there enough money for this? You know, we worked with a small company that had a promising malaria vaccine and we put in grant money for it, we put in

several million dollars of grant money, and we were able to push this forward, but, ultimately, they couldn't get venture capitalists to invest.

On grant money, we can't the lights on and the doors open of companies and you've got to have investors put money into them or else we're not going to get anywhere.

And so I guess I would say yes, there is some grant money--on a side note, it's woefully inadequate--but that's still not going to do it. Even if we put all of that there, it's not going to get us to our goal.

MR. MacDONALD: Melinda, thank you very much, both for the response and that very telling anecdote.

Orin, you work to provide pneumococcus vaccines. Isn't it the case that the R&D on pneumococcus is basically already done? And don't take this as a double-barreled question but what I'm trying to say is what more would an advanced commitment do at this point?

MR. LEVINE: Thanks for that. I think pneumococcus provides us an important example, actually. It's a huge global health problem and a lot of people are probably surprised to find out that WHO estimates that pneumococcus disease kills 1.6 million people a year. That's more, even, than malaria. There's a $2 billion market in developed countries that's been pulling R&D along. We've got clinical trials that show the vaccine's effective in saving lives in developing countries.

And yet a big commitment for industry, even bigger than their R&D commitment, is the investment in capacity. To build a manufacturing plant is hundreds of millions of dollars, and so one of the major things that the advanced purchase contract could do would be to really change that risk for industry and accelerate the ability for us to have the capacity to supply the developing world and save lives immediately against pneumococcal pneumonia.

MR. MacDONALD: Thanks very much.

Michael, you wrote the book or maybe I should say "the books" on this issue. Three billion dollars nonetheless seems like a lot of public resources to promise for something that might never exist. Or maybe it's going to come along anyway. Why don't we just wait and see if that happens.

MR. KREMER: Thanks. Well, as Melinda pointed out, a million people, minimum, are dying of malaria every year, and in that sort of a situation, just advancing the development of a vaccine by a few years, or advancing the distribution of a vaccine could make a huge difference.

We've done some cost-effectiveness calculations and these are available, by the way, on the CGD Web site, if anybody wants to play with them, and change the assumptions. But if you advance development of a vaccine by one year and advance the distribution of it by two years,

this would be extremely cost-effective relative to other public health interventions in the poorest countries.

And I think in terms of us, you know, is this something that we want to spend the money on? Well, if you think about how we get products to the developed world, it's through a combination of "up front" funding, on the one hand, through institutions like NIH, and the promise of a market that spurs private sector competition, harnesses the energy of the private sector.

This is really just trying to do the same thing that we do for developed countries, which for all its imperfections, is yielding lots of new medical products. Take that same combination approach and use it for developing countries.

And I guess just to answer the final part of your question, it's just that, you know, if no vaccine is developed under this, there's no cost through the advanced market commitment, at least there's no cost. If a vaccine is developed, millions of lives are going to be saved in an extremely cost-effective way.

MR. MacDONALD: Thanks very much.

Alice, as CFO for the Vaccine Fund, you've been very effective in mobilizing resources for vaccines in developing countries. How would this proposal fit in with what you are doing of what you would like to do?

MS. ALBRIGHT: Thank you. Many of you are familiar with GAVI and the Vaccine Fund and what our aims are, but for those who aren't, some of our most important goals are to improve the access to vaccines, the availability to vaccines, and also, over time, to improve the security of vaccine supply, and a number of our initiatives actually fund efforts like this, including the one that Orin is leading.

And we have now, to date, raised over $2 billion. Much of that, very generously, has come from the Gates Foundation. I see my Gates friends over there, so thank you. But also very much from U.K. government, the U.S. government, Norway, and a number of others.

So we've raised over $2 billion at this stage and are working on a number of very significant initiatives to raise that number, including what some have mentioned this morning, the IFFIN [ph], which we're also working very close with U.K. government on. The Vaccine Fund in itself is a form of a pool mechanism. We raise long-term money to make long-term commitments through the GAVI process to both investing and infrastructure as well as investing in supplies.

I think one of our biggest characteristics is that we're very flexible. There's very few rules about what we can actually do and I think that's a huge benefit in this regard.

As far as how our work coincides with the pool mechanism's work, we view the pool mechanism's work as being a very promising potential avenue for deploying our donors' funds, and our leadership has read this report, they're extremely excited about it, we very much welcome the work that was done, we think it's a terrific compilation, and I thank Owen, Ruth, John, others, Gargi [ph], for pulling together not only information about the problem, the process, the market, but also the mechanics, and we think it's a tremendous step forward, and I think the next step for us is very much to have wide debates within the GAVI world to see how it could apply to our world. Our world right now is focusing very much on available vaccines but we think the pool mechanisms could possibly be applicable to not only that.

I think John mentioned earlier that there's still significant investment risk in that area and that's something that a pool mechanism could help, particularly this kind.

But also will have real applicability to the newer vaccines that we're also beginning to look at. So we think it coincides very, very closely.

MR. MacDONALD: Terrific. Thank you very much. I want to pause for a moment to thank our extremely distinguished panel for accepting this sort of rapid-fire grilling and thank them for giving answers that are both informative and very crisp.

I'm going to ask one more question of each of you. Then I'm going to start taking questions on cards from the audience. I neglected to say if you'd like to put your name on the card, I'll be happy to read it out. If you want to do it anonymously, that's fine. But I'd be very pleased to acknowledge questions and it will also help Owen, when he goes to reply on the blog, to note where the questions came from.

And if you turned in a card and didn't put your name on it, you can turn another one in later with your name, if you like.

Rudi, how would an advanced market commitment change the number and types of deals that larger firms might look to make with biotechs and emerging suppliers? I'm going to give you 90 seconds for that. It's a hard one.

MR. DAEMS: Yeah; okay. I'll be very brief there. Actually, there are two points there in the relationship. I believe that we're going to see an intensified relationship between large pharmaceutical companies and biotech.

In particular, when it comes to the first, what you're addressing is the R&D. For quite some time now, Big Pharma knows that all innovations do not come out of their own labs. It is an ongoing process that they have these strategic alliances with biotech companies, often based on the royalty payments, and so on.

So, in short, what I'm saying is that even if the real expertise to pull this off, this major project, developing a product against malaria, for example, from A to Z, is a task that will be undertaken by large companies. There's a big, big role to played for small biotech companies.

The second part of your question was about manufacturing. That's a different ball game. Actually, I believe that, and ultimately I hope also, that developing countries will be in a position to not only develop molecules like this themselves, which they are unable to do at this point in time, but at least they can come in on the tail-end side, and if you're going to truly have a kind of a Marshall Plan in which we have large volumes of vaccine being produced, it better be done locally.

So, again, I expect Big Pharma, in particular, over here, to have strategic alliances, if not joint ventures with emerging economy suppliers.

MR. MacDONALD: Thanks so much.

Orin, what's so special about vaccines? this is not a double-barreled question but I'm going to explain it.

If this is such a great idea, why aren't we doing this for microbicides and for antibiotics and all kinds of other life-saving drugs?

MR. LEVINE: Well, personally, as a person in public health, I can't say that you shouldn't, but I think there are things that make vaccines special. For me, vaccines are the ultimate in sort of social justice. That if you look at what our experience has been with vaccines in the U.S., we've essentially eliminated racial inequality in the instance of diseases like pneumococcal disease and HiB through the application of vaccines, and I think they hold the same potential for developing countries.

That the inequalities and disease burden that we observe today can be greatly diminished or even banished through the widespread application of vaccines, and I think it's their high degree of effectiveness, their simplicity and their ability to address sort of fundamental justice issues that make them unique.

MR. MacDONALD: Thank you, Orin.

Melinda, as I understand it, a lot of the research on malaria is being done in universities and government research centers, and I imagine that people there are not motivated, especially by the availability or lack of availability of a market.

So would this really make a difference to vaccine, to the search for a malaria vaccine?

MS. MOREE: The thing about products is that it's companies who make products, and so every vaccine I've ever gotten, I've gotten a lot of them because I travel all over the place, every vaccine that my kids have gotten have come from a company.

And so, you know, the innovation happens oftentimes in academic research institutions and in places like the National Institutes of Health, and there's great work going on there for malaria vaccines.

But great research doesn't actually save kids' lives directly. It's products in their arms that save their lives and it's companies who take that piece of the whole innovation chain and make the products.

And so what we've seen in malaria is that there's lots of work in the academic and government realm but very, very little in that place that takes those good important discoveries and turns them into real products.

And so that's where I see something like this could be helpful. When we sit and talk with companies, and we've talked to a lot of them, we talked to scientists and they're thrilled, you know, the holy grail of a malaria vaccine, that's a great thing to work on. Everybody wants to be a part of something that's of great significance.

But then you sit down with the market people and the senior business people and it's like, yeah, but where's the end game here?

We make a malaria vaccine, it's mostly poor people who need it, and there's just no way for us to make a return on our investment here.

And so it's going to get deprioritized. I've talked to companies again and again, where that happens. I have to believe that if we could address some of the market issues, that many of these companies would move more into this realm of working on a malaria vaccine.

MR. MacDONALD: Thank very much, Melinda.

Alice, my next question for you actually was on my sheet and it's also the first one that's come up from the audience. So we're starting to merge into the situation where we have questions from the floor.

I learned from the report, that about three-quarters of the world's children are currently protected from diseases such as diphtheria and polio and that saves about 3 million lives a year.

But we also heard from Mark Feinberg of Merck, that 3 million children die of vaccine-preventable diseases each year because they have not been vaccinated.

What guarantee do we have that this new mechanism would ensure delivery of the vaccines to those who need them most?

MS. ALBRIGHT: I think that's a very complicated question and we don't necessarily have all the time to answer it. But I think we see the opportunities and the needs really falling into several different areas. Clearly, vaccine-preventable, existing vaccines are a huge priority for us, and, frankly, they represent the biggest amount of money that the Vaccine Fund and GAVI spend right now.

To date, we have saved 670,000 children and we have vaccinated millions, millions more against a range of diseases, and for us that's really a huge focus.

But I think sort of at the core of your question is why should we be spending money on vaccines that don't exist yet when there is all this immediate problem, and I think we have to do both.

I mean, the scale-up time, as you've heard from a number of the presentations today, the scale-up time for new vaccines is considerable.

It's also considerable across a number of constituencies. It's considerable, obviously, for today from industry's side, it takes years to get vaccines developed, produced, manufactured.

It's also considerable from a country's perspective and that's one of the lessons that we're finding out within GAVI, is it takes a long time to create and fund and mount a successful immunization effort in these countries.

So I think from the an investment perspective, we really do need to stress both, both the existing vaccines as well as the new vaccines.

MR. MacDONALD: Thanks very much.

Michael, a lot of these questions, when I was a journalist, we would have called them softball questions. You know, don't you love this? Yeah, we love it. So I'm going to ask you one that's, you know, what's the downside to this? What are the risks? There's nothing that's perfect, I imagine, in the world. Tell us about the problems.

MR. KREMER: I think the challenge in putting together this advanced market commitment is getting the details right. On the one hand, you have to make your commitment credible to industry or else industry's not going to invest.

On the other hand, as John pointed out, you have to make sure that you're promising to buy a product that's actually going to work in the field and is actually going to be used by the governments that need it.

And the details of how you design it are going to be critical to whether you can achieve both those objectives. Rachel Glennerster and I discuss a lot of these details in our book, Strong Medicine, in the working group report, and the working group spent a huge amount of time trying to think about those details.

And I think, as John pointed out, sort of the combination of some technical specifications, some indication that developing countries really want it, and some adjudication committee to determine whether the specification's been met, and that adjudication committee being trusted by all parties, is going to be critical to making this work.

At the same time, I want to highlight the risks of not doing anything. If you look at the 1200 new products that have been developed, only thirteen of them were for tropical diseases, and if you look at, some of those were actually developed for veterinary purposes and then found human applications.

As was pointed out, these investments take a long time and there's a huge risk of failure. If we want these vaccines for the future, then we're going to need to start the investment now. To start the investment now, we need to give firms some indication that they're actually going to be able to sell the product at a price that's going to be able to make this attractive commercially.

And to get that process going, we need to make some commitment to firms today.

MR. MacDONALD: Thanks very much, Michael.

Melinda, now I'm on to the sort of wild territory of scrawled questions, some are more legible than others, there are points for legibility because if I can read it, then I can ask it.

But here's one that actually really intrigued me, and I'd like Melinda, maybe you to start off, and then if somebody else wants to add their 15 seconds to this.

Why not just build a generic vaccine industry from the start to capitalize on government and philanthropic vaccine development?

MS. MOREE: It's an option. You know, this has been done in some developing countries. The vaccine manufacturers are publicly owned and run vaccine plants. I think that most of our experience would show that the public sector doesn't do this very well. Now you could say could you do something different and build in the incentive in the sense of urgency and all these other pieces. Well, that looks kind of like a company.

So I'm not sure, actually, where we benefit from that.

I do think, though, that what something like this will do, if we fix the market--so industry said you don't buy the vaccines we use now. Okay. Vaccine Fund. We started buying the vaccines we need now.

But yeah, but these new vaccines are going to be more expensive; you're not going to buy those. Put an advanced market mechanism into place. Now if that doesn't work, we're a little out of options, and so that's saying that we're losing the ability to figure out some way to work with industry.

I think at that point we may have to look at, okay, do you just invest and build something? But it wouldn't be the first place I'd start.

MR. MacDONALD: Anybody want to add to that? Or I've got some other questions here. Since this proposal is not an "up front"

payment, how will the mechanism speed up the time of vaccines to market? Isn't this just determined by scientific capabilities?

Michael, do you want to talk to that?

MR. KREMER: Sure. If you look to [inaudible] and we've heard some discussion of this earlier. Vaccines like Hepatitis B or haemophilus influenzae b, there's huge delays in getting this from the rich world market to the poor world market, 15 years, and given the number of people dying from this disease every year, this is a huge number of lives that have been lost, and one of the reasons why this happens is that companies aren't--they're not willing to immediately start building infrastructure to serve these markets when they don't know whether the market's going to be there, and when there's pricing issues about can they make this a viable market for themselves, given the rest of their pricing.

What this is proposing to do is instead of having a relatively small market with high prices from the beginning, they immediately go to a much larger market with somewhat lower average prices but greater total revenue, and this could make it attractive for firms, not just to start out by serving the rich countries but also to serve, really, the entire world. Let me just, to pick up on what you said, this really is a case of global equity because vaccines are something that are really a product that are very deliverable in poor countries.

That's why 75 percent of kids worldwide are getting vaccines, and even in Africa, the poorest continent, more than half of kids get the basic vaccines.

I should stress that all of the cost-effectiveness analysis that was done is based on existing vaccine rates or small projections of departures from that.

MR. MacDONALD: Thank you so much. Alice, I think this falls in your bailiwick but if somebody else wants to speak to it, please let me know.

How can this initiative guarantee that particularly among the poorest of the poor in the developing world, a demanding, informed, and organized population exists.

The polio vaccine, once made available, took decades to be widely used. After all these incentives and R&D take place, are you, and I guess by that they mean all of us who are in favor of this, going to leave it up to government to disseminate information, train, and provide infrastructure and educate the multitude of audiences that are needed for distribution and use of the vaccine?

MS. ALBRIGHT: That's also a huge question for a short amount of time. One of the things that GAVI has dedicated a lot of work towards is actually educating and working with countries to help them actually get trained and scale up immunization efforts.

GAVI is fundamentally a very country-owned process. The application process is very much initiated at the country level and as the ministries of health working with their people, and their own constituencies, to try to devise and set their own milestones an then implement the program.

But you're absolutely right. I mean, getting people trained is a critical, critical challenge.

I would actually also like to ask Orin to say something because I think that the work that you guys are doing in the ADIP projects is very much sort of along these lines.

MR. LEVINE: Yeah. I mean, I think one of the fundamental challenges that we've had in trying to achieve the successes that we now take for granted with things like polio vaccine is that we've had to build recognition in many of these places of the burden of these diseases.

Most of the places where most of the children die, there is no laboratory capacity, they die, but people don't know what they die of. And so if you go to them and say we have a new life-saving vaccine that can prevent pneumococcal disease or polio infections but they never knew that it was a pneumococcus or a polio virus that was killing those kids, there's no value assigned to the vaccine, and so I think it's really important that we remember that advanced purchase contracts are an important treatment for one ailment in the process, but that there are other parts of the process that need care and investment as well and part of that is creating awareness of the disease and the value of the vaccine.

MR. MacDONALD: Thanks very much.

I'm going to do just two more questions and then if anybody has something really burning to say, that they didn't have an opportunity to say, I'll give you a moment, but I think given our time, not going to let everybody or invite everybody to make closing remarks.

But here's a question I find particularly interesting and it's in fact the only one so far with a name on it that I can read.

It's from--and I don't know this gentleman--Louis Salacup [ph], perhaps, of NIH, and Louis asks: Is it really true that markets are not big enough with the increases in the GAVI funding and funding from public-private partnerships? And I wonder, Rudi, if maybe you would be the one to answer that question.

MR. DAEMS: It's a tough one also but, actually, to me, basically, it goes down to what are your choices in incentivizing R&D from suitable R&D? I agree with Melinda that probably it needs a public-private partnership.

The difference here I see, and that is a great truth of this proposal at least, is there are basically two ways, and Professor Kremer has described this very well, is a push and pull mechanism, and I know

that there are two kinds of ideas and people will rally around one of these, and to me they're not mutually exclusive, to start with.

But if I've got to believe in one of them being the overriding, driving factor that would pull all of this true, it is for the first time in the way it has been presented here today, this AMC proposal.

MR. MacDONALD: Thank you very much.

Melinda, did you want to add something to that?

MS. MOREE: I just want to add that, you know, the issue of markets in the developing world is largely driven by dogma. So we set out to actually see if we could put some evidence behind this and we hired Boston Consulting Group to go out and do a little area market, malaria vaccine market assessment, and, you know, to cut to the chase, essentially what it shows is that it's not a market that's going to incentivize companies to make a malaria vaccine, and if you take away government funding of a malaria vaccine and think about the more expensive vaccines that are coming along, you essentially get almost no uptake of the vaccine.

So if you're a company and you look at this, and you're looking at your end game, it's just not readily apparent, and so what we're trying to do I think in these whole efforts is to say let's stop talking dogma, say there are no markets, where are there markets? where are there not? and then let's do something about fixing them.

It might be different for different vaccines. We don't think the malaria vaccine that we can make, that will protect kids will protect travelers. So we don't have those markets to tier prices off of. It may be different for HIV or other ones who may need different solutions.

Again I think that's one of the downsides in the advanced market mechanism. If we don't tailor them, we'll make mistakes. But I think that more and more, we do need to go out and answer those questions. Are there markets? Are there not? Where we've looked hasn't looked really promising.

MR. MacDONALD: I don't know that we'll get a better wrap than that but if there's somebody who thinks they can top what Melinda has to say, please do so.

MS. MOREE: Now there's a challenge!

MR. MacDONALD: If not, I'll read one other question but I'm going to leave it hanging there because I want to encourage you to go to our Web site, cgdev.org, and click on Owen Barter's remarkable blog.

Those of you who have not seen it yet are in for a real treat because he not only provides information about this proposal but tracks virtually anything that moves, that has anything at all to do with vaccine development. He's been at it for some time and it's a very, very rich source of information.

In your packets today, you have an interview that he did on the feasibility of the U.S. making this commitment, it's two pages, I found it incredibly enlightening, and that's the sort of treasure that you find on Owen Barter's blog site.

You will see Owen's picture on the blog but I also want to point him out. Here, this is the guy, and during refreshments, I urge you to seek him out, and also when you visit the blog it's really easy to post your comment and I would like to encourage you to do so. You can either do it in your personal capacity or on behalf of your organization. But you might want to make that clear, if it's the ladder.

One of the questions that Owen is going to be dealing with on the blog: Some people say that public health services are a shambles in many of the poorest developing countries. How will this be addressed by the model of an advanced market commitment? So stay tuned for that.

Nancy, I'm going to turn it back to you for final remarks. Thank you very much and could I please have a found of applause for our magnificent panel. Thank you so much.

MS. BIRDSALL: Thank you all for staying this long. I don't want to keep you more than another minute from the reception. There is a reception afterwards. But I want to end by recalling something Rick Klausner said at the beginning, which is the importance of keeping the conversation going, and as the morning proceeded, I wrote down two steps that seem important to me, to keep the conversation going, in which all of you can participate and help.

The first is that as is the case with so many great challenges in the world, we have to consolidate the technical consensus. I think this report takes us 99 percent of the way but there will still be some details for specific vaccines under specific situations.

The second step--and it has to come simultaneously, and that's my point actually--is that we need to create a sense of urgency at the political level, to move this idea forward to action.

It has to come simultaneously because we know from experience, in the development community, that the final dirty details only really get worked out when the political momentum is there, and I was thinking about the tremendous success of the debt relief movement.

Those of you who are active in the development community will know exactly what I'm talking about.

The final stages of what exactly to do, in which countries, how much debt to relieve, are still actually being worked out. But the political momentum began to build in the mid '90s and it kind of exploded around the jubilee year of 2000.

So we need to simultaneously work on the technical consensus and at the political level.

Now we know that the United Kingdom, which is hosting the G8 summit in Gleneagles in July, we hope will put the idea of an advanced market commitment on its agenda.

I think the key issue for those of us, particularly many of you in the Washington community, is to think about U.S. support.

I don't believe, without some U.S. leadership on this issue, public and private, that it can be possible to really consolidate this political momentum.

Now the question is how can all of us participate in both the technical consensus building and simultaneously developing that political momentum?

Well, one idea, one step is we really do urge all of you to go to the blog, raise your tough questions, develop the information, learn more, and read, of course read the report.

Second, do tell others in your organizations. We have an impressive group of people here, you're leaders of your own institutions and organizations, active participants. We're very happy to provide any of the speakers we had today, of our keynote speakers, our panelists, staff of CGD, if you want a speaker to talk more about this and answer more questions.

I think those are the key things.

Third, if you're a member of the Washington policy community, you have influence, and some of you do on the Hill, in the executive branch--ask us to help you sort out how you can help us move this message into the political realm, capture the moment that I believe will come out of the G8 meeting, and in the end, put that light back into the mothers' eyes who are losing their babies in the developing world.

Thank you very much. Reception. Start the conversation now.

[END OF TAPED RECORDING.]

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